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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,225	03/17/2006	Ashfaq Mahmood	58345(70207)	5276
21874 7590 06/18/2010 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
RIDER, LANCE W				
ART UNIT		PAPER NUMBER		
1618				
MAIL DATE		DELIVERY MODE		
06/18/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/534,225

**Applicant(s)**

MAHMOOD ET AL.

**Examiner**

LANCE RIDER

**Art Unit**

1618

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 March 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 16-21, 24, 29-32, 34, 40, 46-48, 54, 63-65 and 69 is/are pending in the application.
- 4a) Of the above claim(s) 36, 40-43, 46-48, 54, 63-65 and 69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-21, 24 and 29-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-940)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### **Status of the Application**

The remarks and amendments filed on March 24<sup>th</sup> 2010 are acknowledged. Claims 16-21, 24, 29-32, 36, 40-43, 46-48, 54, 63-65, and 69 are currently pending, claims 1, 5, and 11-13 have been canceled, and claims 36, 40-43, 46-48, 54, 63-65, and 69 have been withdrawn with traverse due to the election requirement filed on September 8<sup>th</sup> 2009. Applicants also elected the species of the compound N-(2-Mercapto-ethyl)-2-((2-mercapto-ethyl)-[3-(4-phenyl-piperidin-1-yl)-propyl]-amino)-acetamide with a rhenium ion bound.

### **Response to arguments**

### **Withdrawn Rejections**

Receipt and consideration of Applicants' amended claim set and remarks filed on March 24<sup>th</sup> 2010 is acknowledged. The rejection of claims 16-21, 24, 29-32 under 35 U.S.C. 103(a) as being unpatentable over Meltzer et al., U.S. Patent 6,171,576 in view of Largent, B. L., (The American Society for Pharmacology and Experimental Therapeutics, 1987) is withdrawn. Applicant's argument that Largent teaches sigma receptors and not dopamine receptors bind to the 4-phenylpiperidine moiety, and that Meltzer teaches dopamine transporter ligands bound to a metal chelator and not dopamine receptor ligands is found persuasive.

**New Grounds of Rejections**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

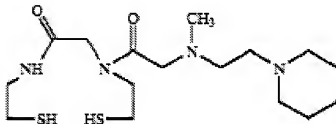
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 16-21, 24, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over John et al., U.S. Patent 5,919,934 in view of Largent, B. L., (The American Society for Pharmacology and Experimental Therapeutics, 1987).**

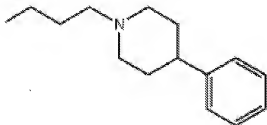
John teaches sigma receptor imaging agents with a metal chelating group linked to a sigma receptor ligand (i.e. piperidines linked to metal chelators, shown below). (See column 12, line 25.)



John teaches that the linker between the metal chelators and the sigma receptor ligands (piperidine) can be varied and include linkers of CH<sub>2</sub>-N-CH<sub>2</sub>, the identical length of applicants claimed linker (a propyl chain). John also teaches the use of Rhenium and radionuclides as the metals in these imaging agents. (See column 5, lines 63-67.)

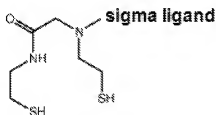
John does not disclose the dopamine ligand is a 4-phenylpiperidine (the ligand portion of the currently elected species).

Largent discloses that the affinity of sigma receptors for ligands is primarily associated with the 4-phenylpiperidine moiety (shown below). See the abstract and Table 1, page 777.

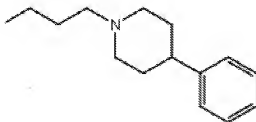


Largent further teaches that the 4-phenylpiperidine can be connected to an n-propyl chain and binds tighter when substituted at this position.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to combine the metal chelating agent disclosed by John with the sigma ligands disclosed by Largent in order to obtain a sigma receptor imaging agent. John teaches a metal chelator linked to a sigma receptor ligand.

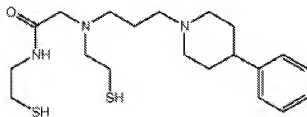


Largent teaches that n-propyl-4-phenylpiperidine is a good sigma receptor ligand.



The replacement of one art recognized sigma ligand (such as the piperidine disclosed by John) with another art recognized sigma receptor ligand (such as the 4-

phenylpiperidine of Largent) is merely a substitution of one art known element for another known in the field. The skilled artisan would have had a reasonable expectation of success for this substitution, given that both of the ligands were known to target the same receptor, both were known to be capable of modification at the N position without losing significant binding affinity, and both ligands have very similar structures. The compound formed (shown below) meets the limitation of the currently elected species and the limitations of the Markush groups of claims of 16-21, 24, 29-32.



### **Conclusion**

No claims allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/  
Examiner, Art Unit 1618

/Jake M. Vu/  
Primary Examiner, Art Unit 1618